UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,847	12/12/2000	C. Frank Bennett	ISPH-0524	4732

26259 7590 09/15/2004

LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/734,847	BENNETT ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Claim Rejections - 35 USC § 103

1. Claims 34, 35, 38-43, 48, which are re-statements of claims 1, 2, 6-11 and 16, and new claims 49, 53, 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. in view of Buchardt et al. for the reasons of record detailed against claims 1, 2, 6-11 and 16 in the office action dated March 31, 2004. Claims 49, 53, 56 and 57 have been added to this rejection because they recite limitations (modifications that increase binding and nuclease resistance, backbone modifications other than phosphorothioates and backbone modifications that are PNA) that are encompassed by the teachings of Anderson et al. and Buchardt et al. and would have been rejected in the previous action if they had been presented at that time. Applicant's arguments traversing the rejection in the reply filed on June 25, 2004 have been fully considered but they are not persuasive.

2. Applicant argues that the Anderson and Buchardt references do not teach or suggest the use of antisense compounds comprising one or more peptide nucleic acid (PNA) modifications to modulate the processing of wild-type cellular mRNA targets. Applicants assert the compounds taught by Anderson et al. are directed to viral mRNAs and not wild-type mRNAs. However, although the working examples taught by Anderson et al. are directed to viral targets, use of PNAs against other types or mRNAs

are contemplated in the specification. On page 5, lines 6-7, Anderson et al. teach that "PNAs can ideally be used to target RNA and ssDNA to produce antisense-type gene regulating moieties." This is not a limiting statement and would encompass wild-type mRNAs. On page 8, lines 30-32 Anderson et al. teach that PNAs are useful drugs for diseases like cancer, in addition to treatment of viral infections. Buchardt et al. teach the use of PNA compounds as antisense and state that such compounds have the advantages enumerated in the previous rejection.

3. Additionally, Buchardt et al. state at column 20, lines 56-column 21, line 6: that in addition to viral targets, PNAs can be used against targets such as "intracellular adhesion molecules (ICAM), 5-lipoxygenase (5-LO), phospholipase A.sub.2 (PLA.sub.2), protein kinase C (PKC), and RAS oncogene" and also PNAs can be used to treat diseases such as "ocular, skin and systemic inflammation; cardiovascular disease; cancer; asthma; psoriasis; cardiovascular collapse; cardiac infarction; gastrointestinal disease; kidney disease; rheumatoid arthritis [and] osteoarthritis". These targets are normal parts of cellular machinery and as such would be translated from wild-type mRNA and these disease states are not virally caused.

Claim Rejections - 35 USC § 112

4. Claims 34-63 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record detailed against claims 1, 2, 4-16 and 31-33 in the office action dated March

31, 2004. Applicant's arguments filed June 25, 2004 have been fully considered but they are not persuasive.

5. Applicant argues that the instant specification is enabled for *in vivo* therapeutic uses and the art references used for support of a rejection of non-enablement are not sufficient to demonstrate the unpredictability of antisense therapeutics. Applicant has suggested that the examiner has focused on small parts of the cited references while ignoring the whole. This is not the case, the quoted sections are used to support an assertion that use of antisense therapeutics is not routine and each of the cited references supports such a position. Applicant argues that the cited references "actually teach the *potential* usefulness of this class of drugs" (emphasis added). This is correct, the references teach that antisense drugs have the *potential* to be useful, which is why the application has not been rejected under 35 USC 101, but the state of the art at the time of filing was such that *in vivo* applications were not routine. While the quantity of experimentation needed to perform any one aspect of the steps needed to take a test compound from *in vitro* to *in vivo* applications may not be sufficient to prove lack of enablement, a large quantity of experimentation needed for each and every step is more likely to constitute undue experimentation. The most well-designed *in vitro* experiments may still not work *in vivo* because efficacy *in vivo* is not the only factor to be considered: delivery of nucleic acid therapeutics *in vivo* has never been considered to be routine.

6. With regard to the difficulties of delivery, Jen et al. state (see page 313, second column, second paragraph) "One of the major limitations for the therapeutic use of AS-

ODNS and ribozymes is the problem of delivery.... presently, some success has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable".

7. Delivery of nucleic acid-based therapies remains an obstacle at the present time. Given that it is still a formidable challenge, in order to practice the claimed invention *in vivo* a number of variables would have to be optimized, including 1). the mode of delivery of the oligonucleotide to an organism that would allow it to reach the targeted cell, 2). the amount of oligonucleotide that would need to be delivered in order to allow inhibition of the expression of a target gene once it reached the proper cell and 3). ensuring the oligonucleotide remains viable in a cell for a period of time that allows inhibition of the gene to an extent that there is a measurable and significant therapeutic effect. Each one of these variables would have to be empirically determined for each antisense oligonucleotide. While optimization of any single one of these steps may be routine, when taken together the amount of experimentation becomes such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore it is unreasonable to believe that applicant at the time of invention was able to overcome these challenges and practice *in vivo* therapeutic methods.

8. Applicant states the amended claims of June 25, 2004 obviate the previous 112 rejection by reciting *in vitro* applications and request withdrawal of the rejection. The examiner sees nothing in the amended claims that narrows the scope of the claimed method to encompass only *in vitro* applications; the rejection of record is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

(EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
September 3, 2004

SEAN McGARRY
PRIMARY EXAMINER
1635